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Symptom dimensions and functional impairment in early psychosis: More to the story than just negative symptoms

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ABSTRACT

Functional impairment is a defining feature of psychotic disorders and usually appears well before their onset. Negative symptoms play a prominent role in the impaired functioning of individuals with schizophrenia and those at clinical-high-risk (CHR) for psychosis. Despite high rates of depression and anxiety in early psychosis, few studies have examined the contribution of these symptoms to functioning in the putative 'prodrome.' In the current study, we tested the hypotheses that 1) worse negative and disorganized, but not positive, symptoms would be significantly related to impaired social and role functioning in two cohorts of CHR individuals (combined $N = 98$) and a separate sample of individuals with recent-onset (RO) psychotic disorders ($N = 88$); and 2) worse anxiety and depression would be significantly related to impaired functioning in both samples, above and beyond the contributions of negative and disorganized symptoms. Findings largely supported our hypotheses that more severe negative and disorganized symptoms were related to poorer social and role functioning in both samples. Anxiety and depression severity were significantly related to poorer functioning in both samples. In addition, depression, but not anxiety, predicted poorer global and social functioning above and beyond that explained by negative symptoms in the CHR sample. These results suggest the need for phase-specific treatment in early psychosis, with a focus on symptom dimensions to improve functional outcomes for CHR individuals.

1. Introduction

The longer individuals with schizophrenia are left without adequate treatment, the worse their symptoms and functioning become (McGlashan and Johannessen, 1996; Keshavan et al., 2003). These findings prompted research addressing the urgent need to identify those at clinical high risk (CHR) for psychosis. Longitudinal studies of adolescents and young adults with CHR syndromes, primarily those with attenuated psychotic symptoms, show a mean transition rate to full psychosis of 29% over two years (Fusar-Poli et al., 2012). Given that the majority of CHR individuals do not convert within this time period, however, researchers have discussed the risk-to-benefit ratio associated with treatment during this phase (Haroun et al., 2006).

Recently, CHR studies have moved beyond a singular focus on psychotic transition outcomes, exploring the relationship of clinical symptoms and other risk factors to real-world functioning. Functional impairment is present in CHR individuals compared to healthy controls (Cornblatt et al., 2007; Addington et al., 2011) and predicts later psychosis (Cannon et al., 2008; Velthorst et al., 2010; Dragt et al., 2011), but is also present to a significant degree in CHR individuals who do not go on to convert over time (Schlosser et al., 2012). Moreover, poor functioning may be relatively stable in a subset of CHR individuals regardless of changes in their positive symptoms. That is, some CHR individuals who begin follow-along studies with poor functioning continue to show poor functioning after several years, even when their positive symptoms never cross the threshold into full psychotic severity (Yung et al., 2007; Addington et al., 2011; Schlosser et al., 2012). Thus, although they do not convert to full-blown psychosis over brief follow-up periods, these 'false positives' are still in need of clinical intervention.

Numerous studies have shown that symptoms contribute significantly to impairment in individuals with schizophrenia (Norman et al., 2000; Pinikahana et al., 2002), with negative symptoms accounting for up to 18% of the variance in functioning (Ventura et al, 2009). Similar findings have been replicated in CHR individuals (Niendam et al., 2006b; Cornblatt et al., 2007; Niendam et al., 2007; Svirskis et al., 2007; Corcoran et al., 2011), and negative symptoms are a significant predictor of conversion to psychotic disorder (Piskulic et al., 2012). In addition, disorganized symptoms are related

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to impaired functioning in psychosis (Norman et al., 1999; Sakiyama et al., 2002; Takahashi et al., 2005). A recent study on a small sample of CHR individuals showed that disorganized symptoms were a significant predictor of declines in social functioning over a one-year follow-up (Eslami et al., 2011).

Depression and anxiety are also highly common in schizophrenia, with an estimated 30 to 40% of individuals meeting criteria for a major depressive episode and 11 to 15% with a diagnosed anxiety disorder (Sands and Harrow, 1999; Achim et al., 2011). Depression and anxiety often precede the disorder (Yung and McGorry, 1996; Häfner et al., 2002), and are associated with poorer functioning (Dickerson et al., 1998; Häfner et al., 1999; Braga et al., 2005; Saarni et al., 2010). High rates of comorbidity have been a recent focus of CHR research (Salokangas et al., 2012; Fusar-Poli et al., 2013). One common finding across research clinics has been the high prevalence of depression and anxiety, with rates of major depressive disorder ranging from 17 to 50% and anxiety disorders from 24 to 58% (Meyer et al., 2005; Rosen et al., 2006; Salokangas et al., 2012), and these symptoms are related to less functional recovery over time (Schlosser et al., 2012). Thus, it is possible that the functional impairment in this population may be related, at least partly, to symptoms of depression and anxiety. No studies to date, however, have examined the relationship of both depression and anxiety to functioning in the context of other symptom domains in early psychosis.

In the current study we examined the impact of various symptom domains on functioning in two cohorts of CHR participants—one assessed at the UCSF Prodrome Assessment, Research and Treatment (PART) and the other at the UC Davis Early Diagnosis and Preventive Treatment of Psychotic Illness (EDAPT) programs. We also examined the relationship between symptoms and functioning in a sample of participants at UCSF with a recent onset of psychotic disorder (RO), for context and comparison. We hypothesized the following for both CHR and RO samples: (a) more severe negative and disorganized, but not positive, psychotic symptoms would be negatively related to functioning; and (b) symptoms of depression and anxiety would explain unique variance in functioning, above and beyond the variance explained by negative and disorganized symptoms. Of note, these data were originally collected in separate studies (CHR vs. RO) for separate purposes by the authors as part of an established collaboration. Hypotheses were developed prior to examining any data or conducting analyses, based on available measures.

2. Materials and methods

2.1. Participants

We recruited 186 participants aged 12 to 28 years from the community via advertisements and referrals at the UCSF PART (CHR $n = 65$; RO $N = 88$) and UCD EDAPT ($n = 33$) programs for a variety of research studies. The majority of participants are referred by treatment providers, educators, hospitals, or family members who have been made aware of our programs by word of mouth, through our websites, and regular community outreach presentations we provide for schools, clinics, and other treatment programs. The socioeconomic makeup and ethnic makeup of the PART and EDAPT programs are representative of the diversity of the larger San Francisco and Sacramento communities. The PART and EDAPT programs are largely parallel programs in terms of study criteria and procedures. We included two sites of CHR participants to achieve adequate statistical power through a sufficiently large sample size to detect significant effects in the proposed regression analyses. Inclusion as a CHR participant at either site was defined as meeting criteria of a prodromal syndrome on the Structured Interview for Prodromal Syndromes (SIPS; McGlashan et al., 2001). These criteria include one or more of the following: 1) Attenuated Positive Symptom syndrome (APS: attenuated symptoms of psychosis with recent onset or worsening; 94.9%), 2) Brief Intermittent Psychotic Symptom syndrome (BIPS: fully psychotic symptoms of brief duration and with full recovery; 5.1%), or 3) Genetic Risk and Deterioration syndrome (GRD: a decline in role functioning and either a diagnosis of Schizotypal Personality Disorder or a first-degree relative with a psychotic disorder; 2.0%). CHR individuals are recruited at both UCSF and UCD to participate in ongoing studies examining the longitudinal course of psychosis risk, with conversion to psychosis (defined as both affective and non-affective psychotic disorders) as a primary outcome. Inclusion as an RO participant at UCSF was defined as meeting DSM-IV-TR criteria for schizophrenia (70.5%), schizoaffective (26.1%), or schizophreniform (3.4%) disorder with onset within the last 5 years (median number of months since onset = 13.5; range = 0–57). Exclusion criteria were the following: significant current substance use disorder, neurological disorder, or IQ below 70. In general, RO participants were symptomatically stable. That is, current symptoms were in the low-to-moderate range on all measures, no participant had been hospitalized within the past three months, and those taking psychotropic medications were all on a stable dose. Table 1 lists the demographic information for both samples, as well as tests of differences in demographic and symptom variables between the two CHR samples.

2.2. Measures

We assessed CHR status using the SIPS and baseline Axis I diagnoses using the Structured Clinical Interview for DSM-IV (SCID-I/P; First et al., 2002) or, for participants under age 16, the Kiddie-Schedule for Affective Disorders and Schizophrenia (K-SADS; Kaufman et al., 1996). To assess for psychotic symptom severity in the RO participants, we used the Scale for the Assessment of Negative Symptoms (SANS; Andreasen, 1983) and Scale for the Assessment of Positive Symptoms (SAPS; Andreasen, 1984). To assess for symptoms of attenuated psychosis in CHR participants, we used the Scale of Prodromal Symptoms (SOPS; McGlashan et al., 2001). The SOPS is embedded within the SIPS and yields a total score for positive, negative, disorganized and general symptoms. In line with the work of Liddle (1987), and consistent with previous research (Brekke et al., 1994; Andreasen et al., 1995; Barch et al., 2003; Klaassen et al., 2011), we separated the SANS, SAPS, and SOPS psychosis symptoms into the three major factors: 1) Reality Distortion/Positive Symptoms; 2) Disorganization; and 3) Poverty/Negative Symptoms. We used the Brief Psychiatric Rating Scale Depression and Anxiety items (BPRS; Overall and Gorham, 1962) to assess for depression and anxiety in both samples of participants.

Social functioning and occupational functioning were measured using two of the four original items of the Strauss Carpenter Outcome Scales (SCOS; Strauss and Carpenter, 1972): Social Contacts — contact with friends/acquaintances over the past month (SCOS-S), and Useful Employment — time spent employed or enrolled in school over the past month (SCOS-E). We also used the Global Functioning: Social (GFS; Auther et al., 2006) and Global Functioning: Role (GFR; Niendam et al., 2006a) scales, which were developed specifically to capture the range of functioning in CHR or younger psychosis populations. Finally, we used a modified version of the Global Assessment of Functioning scale (GAF; Hall, 1995) as a well-validated, broad measure of functioning. This modified version uses clearly defined anchors to improve reliability and minimize rater bias when making global functioning ratings. Both samples were administered all four functioning measures.

2.3. Procedure

Referred individuals completed a phone screen and, if eligible, were scheduled for an in-person intake interview at the PART lab at UCSF or EDAPT clinic at UCD. After study eligibility was determined via clinical interview with the SIPS (for CHR samples) or SCID-I/P (for RO sample), participants returned to complete the remainder of

Table 1
Sample characteristics, descriptive statistics of rating scales, and differences between sites.

	CHR				RO
	UCSF ($n = 65$)	UCD ($n = 33$)	Total ($n = 98$)	Differences between CHR sites[a]	($n = 88$)
Gender (% male)	58.5	60.6	59.2	0.20	71.6
Age (*M* years [*SD*])	18.74 (4.27)	15.74 (3.41)	17.73 (4.23)	3.50**	21.28 (3.97)
Years parental education (*M* [*SD*])	15.29 (3.21)	14.13 (3.37)	14.88 (3.30)	1.56	15.51 (3.00)
Race (%)					
Non-Hispanic Caucasian	41.5	48.5	43.9	–	44.3
Hispanic/Latino	10.8	15.2	12.2	–	6.8
African-American	6.2	12.1	8.2	–	9.1
Asian-American	18.5	6.1	14.3	–	23.9
Native Hawaiian/Pacific Islander	3.1	3.0	3.1	–	2.3
Multiracial	20.0	15.2	18.4	–	12.5
Positive (*M* [*SD*])	8.75 (3.62)	9.10 (4.15)	8.86 (3.78)	−0.41	3.69 (2.83)
Negative (*M* [*SD*])	13.26 (6.21)	11.74 (5.74)	12.77 (6.08)	1.15	7.68 (3.82)
Disorganized (*M* [*SD*])	8.20 (5.04)	6.21 (3.75)	7.59 (4.75)	1.90	3.60 (2.21)
BPRS depression (*M* [*SD*])	3.38 (1.81)	2.73 (1.42)	3.16 (1.71)	1.82	2.42 (1.61)
BPRS anxiety (*M* [*SD*])	3.52 (1.69)	2.33 (1.38)	3.12 (1.68)	3.50**	3.07 (1.69)
GAF (*M* [*SD*])	46.05 (9.67)	52.88 (10.28)	47.95 (10.79)	−3.20**	44.35 (10.54)
SCOS-E (% full-time school/work)	60.0	87.9	69.4	8.01**	30.7
SCOS-S (*M* [*SD*])	2.54 (1.48)	3.03 (1.31)	2.70 (1.44)	−1.61	2.31(1.53)
GFR (*M* [*SD*])	5.57 (1.96)	6.09 (1.61)	5.74 (1.86)	−1.32	4.74 (1.87)
GFS (*M* [*SD*])	5.75 (1.42)	6.45 (1.28)	5.99 (1.40)	−2.39*	5.25 (1.37)

Note: BPRS = Brief Psychiatric Rating Scale; CHR = Clinical High Risk; GAF = Global Assessment of Functioning; GFR = Global Functioning: Role scale; GFS = Global Functioning: Social scale; RO = Recent-Onset; SCOS-E = Strauss Carpenter Outcome Scales – Employment; SCOS-S = Strauss Carpenter Outcome Scales – Social Contacts.
* $p < .05$.
** $p < .01$.
[a] Site differences for continuous variables were tested using *t*-test, and dichotomous variables were tested using χ^2.

the assessment measures at a second visit. When applicable, caregivers were interviewed during the intake and baseline clinical assessments to obtain collateral information. All assessments were completed by trained research staff who discussed ratings and diagnoses in weekly clinical consensus meetings. Inter-rater reliability was calculated based on staff ratings of training tapes used at both sites, with an average intra-class correlation of .83 for symptom ratings and an average kappa value of .95 for diagnostic agreement.

2.4. Data analysis

To test the effects of demographic variables as potential confounds on the outcomes of interest, we computed bivariate correlations between the functioning measures (GAF, SCOS, GFS, and GFR) and age, gender, and parental education separately for the two diagnostic groups. Demographic variables that were significantly associated with functioning measures were included as covariates in further analyses. We then computed bivariate correlations to test the hypotheses that negative and disorganized, but not positive, psychotic symptoms (SOPS or SANS/SAPS) and symptoms of depression and anxiety (BPRS) would be negatively related to functioning.

To test the hypotheses that symptoms of depression and anxiety would explain unique variance in functioning, above and beyond the variance explained by symptoms of psychosis, we conducted five regression analyses—one for each of the four functioning outcomes (GAF, SCOS-E, SCOS-S, GFS, and GFR)—separately for the CHR and RO samples. In each model we entered the relevant demographic covariates as predictors in step one, then included symptoms of psychosis (SANS/SAPS or SOPS) as predictors in step two, and Anxiety and Depression in the final steps. Predictors were entered hierarchically, but retained in a stepwise fashion in each model if they had a *p* value less than .05. Results of the final model of each analysis are presented.

Prior to conducting all analyses, the data were checked for missing points and outliers, and frequency distributions were tested for normality. When data were not normally distributed due to positive skew, we used Kendall's tau-*b* for correlations, as recommended by Arndt and colleagues (Arndt et al., 1999). When distributions were markedly bimodal (e.g., SCOS-E), we created a dichotomous variable and employed logistic regression for binary outcomes. Where two dichotomous variables were correlated (e.g., gender and SCOS Useful Employment), the *phi* coefficient was used. To control for differences in the two cohorts (UCD and UCSF), site was included as a dummy-coded covariate in the regression analyses.

3. Results

Results of the correlation analyses are presented in Table 2. As predicted, negative symptoms were negatively related to functioning in both samples, across all functioning measures (−.19 to −.47, all *p* values < .05). Disorganized symptoms were related to the GAF and GF scales across both samples, but largely unrelated to the SCOS items (with the exception of SCOS-S for the CHR sample; $r = -.29$). While positive symptoms were largely unrelated to functioning in both samples, they had significant negative correlations with the GAF ($r = -.33$) and GFS ($r = -.20$) in the RO sample. BPRS Anxiety and Depression were negatively related to the GAF in both samples (range = −.19 to −.32, *p*'s < .05), and to role functioning on the SCOS-E scale in the CHR sample (−.23 and −.25, $p < .05$).

Similar to the correlation results, regression analyses indicated that negative symptoms were associated with poorer functioning across all functioning measures in both samples (all *p*'s < .05; see Tables 3 and 4). In the CHR sample, disorganized and positive symptoms were not associated with functioning above and beyond the power of negative symptoms. In the RO sample, positive and disorganized symptoms were associated with lower GAF scores (*B*'s = −.97 and −.80, respectively). Additionally, disorganized symptoms were associated with GFR ($B = -.30$, $p < .001$), and there was a trend for an association between positive symptoms and GFS ($B = -.09$, $p = .05$).

As hypothesized, depression was associated with both GAF ($B = -2.29$, $p < .001$) and GFS ($B = -.16$, $p < .05$) scores in the CHR sample, above and beyond the variance explained by negative symptoms and demographic variables. Depression was not significantly

Table 2
Correlations between symptom and functioning measures (CHR Sample above diagonal, RO sample below diagonal).

		CHR sample									
		GAF	SCOS-S	SCOS-E	GFS	GFR	Positive	Negative	Disorganized	BPRS depression	BPRS anxiety
RO Sample	GAF	–	.22**	.39**	.37**	.35**	−.17*	−.30**	−.24**	−.32**	−.19*
	SCOS-S	.37**	–	.18*	.59*	.20**	.00	−.38**	−.29**	−.10	−.15
	SCOS-E	.30**	.12	–	.24**	.36**	−.12	−.23**	−.07	−.23**	−.25**
	GFS	.57**	.60**	.24**	–	.25**	−.07	−.38**	−.31**	−.12	−.13
	GFR	.54**	.27**	.46**	.46**	–	.01	−.32**	−.20**	−.06	−.06
	Positive	−.33**	−.13	−.06	−.20*	−.15	–	n/a	n/a	.03	.03
	Negative	−.47**	−.27**	−.19*	−.42**	−.45**	n/a	–	n/a	.15	.07
	Disorganized	−.33**	−.08	−.14	−.18*	−.40**	n/a	.n/a	–	−.04	−.05
	BPRS depression	−.24**	−.12	−.04	−.11	−.12	.18*	.02	.07	–	.29**
	BPRS anxiety	−.20*	−.08	.03	−.09	−.09	.15	.04	.06	.51**	–

Note: Positive, Negative, and Disorganized symptoms measured by the SOPS in the CHR sample and by the SANS/SAPS in the RO sample. BPRS = Brief Psychiatric Rating Scale; CHR = Clinical High Risk; GAF = Global Assessment of Functioning; GFR = Global Functioning: Role scale; GFS = Global Functioning: Social scale; RO = Recent-Onset; SCOS-E = Strauss Carpenter Outcome Scales – Employment; SCOS-S = Strauss Carpenter Outcome Scales – Social Contacts.
* $p < .05$.
** $p < .01$.

associated with functioning in the RO sample, though there was a trend for the GAF ($B = -1.07, p = .08$). Contrary to hypotheses, anxiety was not associated with functioning in either sample after controlling for the predictive power of negative symptoms, despite some correlations with functioning. Changing the order of depression and anxiety in the regression equations did not affect the results.

Table 3
Stepwise regression analyses of predictors of functioning in the CHR sample.

	R^2 change	*B* (*SE*)	*t*	*p*
GAF[a]				
(Constant)		62.90 (5.77)	10.90**	.000
Site	Step 1: .09	3.50 (2.03)	1.72	.089
Age	Step 2: .04	−0.30 (0.22)	−1.38	.170
Negative symptoms	Step 3: .13	−0.56 (0.14)	−3.92**	.000
BPRS depression	Step 4: .14	−2.29 (0.52)	−4.39**	.000
GFS[a]				
(Constant)		6.84 (0.52)	13.27**	.000
Gender	Step 1: .07	0.57 (0.26)	2.17*	.033
Negative symptoms	Step 2: .20	−0.10 (0.02)	−4.51	.000
BPRS depression	Step 3: .03	−0.16 (0.07)	−2.11*	.038
GFR[a]				
(Constant)		7.59 (0.49)	15.45**	.000
Negative symptoms	Step 1: .20	−0.13 (0.03)	−4.63**	.000
BPRS depression	Step 2: .00	−0.06 (0.10)	−0.56	.577
SCOS-S[a]				
(Constant)		3.00 (0.56)	5.40**	.003
Gender	Step 1: .12	0.78 (0.28)	2.76**	.007
Negative symptoms	Step 2: .15	−0.09 (0.02)	−4.04**	.000
BPRS depression	Step 3: .01	−0.08 (0.08)	−1.02	.310
		B (*SE*)	*Wald*	*p*
SCOS-E[b]				
(Constant)		8.96(1.85)	23.54**	.000
Site		−0.40(.71)	0.31	.576
Age		−0.29(.08)	13.49**	.000
Negative symptoms		−0.13(.05)	6.21*	.013
BPRS depression		−0.24(.16)	2.20	.138

Note: Statistics of the final model reported; predictors were retained at the $p < .05$ level.
BPRS = Brief Psychiatric Rating Scale; CHR = Clinical High Risk; GAF = Global Assessment of Functioning; GFR = Global Functioning: Role scale; GFS = Global Functioning: Social scale; SCOS-E = Strauss Carpenter Outcome Scales – Employment; SCOS-S = Strauss Carpenter Outcome Scales – Social Contacts; SOPS = Scale of Prodromal Symptoms.
* $p < .05$.
** $p < .01$.
[a] Criterion; linear regression model.
[b] Criterion; logistic regression model.

4. Discussion

The results of our study suggest that, consistent with the schizophrenia literature, negative symptoms are robustly related to impairment in psychosocial functioning, both during the at-risk phase and

Table 4
Stepwise regression analyses of predictors of functioning in the RO sample.

	R^2 change	*B* (*SE*)	*t*	*p*
GAF[a]				
(Constant)		65.79 (2.31)	28.55**	.000
Negative symptoms	Step 1: .40	−1.49 (0.21)	−7.14**	.000
Positive symptoms	Step 2: .11	−0.97 (0.28)	−3.44**	.001
Disorganized symptoms	Step 3: .03	−0.80 (0.37)	−2.15*	.034
BPRS anxiety	Step 4: .02	−0.30 (0.59)	−0.52	.608
BPRS depression	Step 5: .02	−1.07 (0.61)	−1.75	.084
GFS[a]				
(Constant)		6.19 (0.50)	12.51**	.000
Gender	Step 1: .05	0.64 (0.27)	2.36*	.021
Negative symptoms	Step 2: .26	−0.18 (0.03)	−5.54**	.000
Positive symptoms	Step 3: .03	−0.09 (0.04)	−1.98	.052
BPRS depression	Step 4: .00	−0.03 (0.08)	−0.45	.656
GFR[a]				
(Constant)		6.73 (0.61)	11.11**	.000
Gender	Step 1: .04	0.79 (0.33)	2.43*	.017
Negative symptoms	Step 2: .32	−0.22 (0.04)	−5.56**	.000
Disorganized symptoms	Step 3: .11	−0.30 (0.07)	−4.23**	.000
BPRS depression	Step 4: .01	−0.09 (0.09)	−0.97	.338
SCOS-S[a]				
(Constant)		3.57 (0.41)	8.73**	.000
Negative symptoms	Step 1: .11	−0.13 (0.04)	−3.09**	.003
BPRS depression	Step 2: .02	−0.12 (0.10)	−1.27	.209
		B (*SE*)	*Wald*	*p*
SCOS-E[b]				
(Constant)		5.03 (1.80)	7.83**	.005
Age		−0.21 (0.08)	7.24**	.007
Negative symptoms		−0.17 (0.07)	5.47*	.019
BPRS depression		−0.15 (0.16)	0.84	.359

Note: Statistics of the final model reported; predictors were retained at the $p < .05$ level.
BPRS = Brief Psychiatric Rating Scale; Dis = Disorganized symptoms; GAF = Global Assessment of Functioning; GFR = Global Functioning: Role scale; GFS = Global Functioning: Social scale; Neg = Negative symptoms; Pos = Positive symptoms; RO = Recent Onset; SANS = Scale for the Assessment of Negative Symptoms; SAPS = Scale for the Assessment of Positive Symptoms; SCOS-E = Strauss Carpenter Outcome Scales – Employment; SCOS-S = Strauss Carpenter Outcome Scales – Social Contacts.
* $p < .05$.
** $p < .01$.
[a] Criterion; linear regression model.
[b] Criterion; logistic regression model.

shortly after onset of disorder. Also consistent with previous literature, positive and disorganized symptoms did not provide additional predictive power after accounting for negative symptoms and other variables in the CHR sample (Norman et al., 2000; Pinikahana et al., 2002; Niendam et al., 2006b; Cornblatt et al., 2007; Svirskis et al., 2007), while they remained associated with poorer role and global functioning in the RO sample.

This study is the first to report that depression contributes additionally to poorer psychosocial functioning for clinical-high-risk youth. While two previous studies found symptoms of depression to be related to poorer social functioning in CHR individuals, depression did not explain functioning above and beyond negative symptoms (Niendam et al., 2006a; Corcoran et al., 2011). It is important to note that the authors used different measures to assess depression (the BDI in Niendam's study, and the Hamilton in Corcoran's study).

Although depression symptoms showed additional predictive power for GAF scores in our CHR sample, interpretation is made difficult by the fact that the GAF scale confounds psychosocial functioning with symptom severity. As such, we cannot say as to what degree functional impairment is associated with depression specifically versus an artifact of the incorporation of these symptoms into GAF scores. Nonetheless, previous research has shown GAF scores to be driven primarily by role functioning in CHR samples (e.g., Ruhrmann et al., 2010). Also of note, both GAF scores and symptoms of depression are strong predictors of transition to psychosis among CHR individuals (Yung et al., 2004; Amminger et al., 2006; Cannon et al., 2008; Velthorst et al., 2010), suggesting that the relationship of depression symptoms to GAF, in relation to psychosis transition, deserves more investigation.

Symptoms of anxiety were correlated with functioning in both samples; however, they were not associated with impairment above and beyond negative symptoms and depression. Although previous studies have shown a link between symptoms of anxiety and functional impairment among individuals with chronic schizophrenia (Muller et al., 2004; Braga et al., 2005), we know of no studies examining the role of anxiety in functioning of CHR or RO individuals. Anxiety may contribute to functional impairment only in those later on in the course of illness. Alternatively, anxiety in CHR individuals may be secondary to emerging positive and negative symptoms.

Our use of multiple outcome measures revealed interesting patterns between symptoms and functioning, but the variability in results across measures suggests that each may have differing sensitivity to symptom domains in early psychosis. The finding that depression was significantly associated with GAF and GFS, but not SCOS, may be due to the reduced variance on the SCOS items (scored 0–4) compared to the GF (scores 1–10) and GAF (scored 0–100) scales. Indeed, two-thirds of the CHR sample was within 1 point of each other on the SCOS (on the high end of the distribution), while the distributions for the GAF and GF scales were substantially more varied. Only the GF scales were designed for use specifically with this age group and population. Thus, traditional functioning measures such as the SCOS may not be as sensitive in detecting subtle levels of impairment. Further, while the SCOS measures absolute amount of time engaged in role activities or number of social contacts within a specified time frame, the GF scales examine the level of performance given support within the role environment as well as the quantity and quality of social relationships.

Symptoms of depression were associated with functioning above and beyond symptoms of psychosis in the RO sample, but only for the GAF scale. Previous studies of RO schizophrenia have shown a relationship between depression and functional impairment; however, these studies did not account for the potential overlap with symptoms of psychosis using a multifactorial model (Häfner et al., 1999; Sands and Harrow, 1999). An exception is a recent study by Bourdeau et al. (2012) that found depression to predict functional impairment above and beyond negative symptoms among an RO sample, although they measured both depression and functioning via self-report. While we cannot directly compare levels of BPRS Depression scores obtained in the current study with those of previous studies to know if our sample experienced less depression than others, levels in the current study covered the full range of scores. In addition, the GAF conflates symptoms and functioning, with depressed mood putting someone in the 70 or below range. Nonetheless, there may be a floor effect, as the current RO outpatient sample was screened for stability, with generally mild to moderate depression.

Implications from the findings of the current study are limited by the cross-sectional nature of the data. It is unknown whether symptoms of depression and psychosis precede functional decline, or vice versa. In addition, those experiencing negative symptoms are more likely to endorse difficulties with social and role functioning, given the reciprocal nature of these constructs. Future research will benefit from prospective measurement of symptoms and functioning over time. The finding of the relationship between depressed mood and functional outcomes is also limited by the fact that the former was assessed by only one interviewer-rated item. It will be important for future studies to assess depression and anxiety using measures that cover the broad range of symptoms associated with these syndromes. Nevertheless, the BPRS depression item shows strong relationships ($r = .76–.87$) with other well-validated depression rating scales (Addington et al., 1992; Peles et al., 2007). When analyzed in the bivariate correlations, symptoms of depression were significantly related to impairment in global and role, but not social, functioning in the CHR sample; however, when included in a regression that controlled for negative symptoms, depression significantly predicted social functioning. Thus, controlling for negative symptoms as well as gender and site differences may remove some amount of error to reveal the unique relationship between social functioning and depression.

Without follow-up data on the CHR sample, we cannot say whether the relationship holds for truly prodromal individuals, rather than youth with attenuated psychosis who may or may not develop a full psychotic disorder. Thus, it will be important to examine the relationship between symptoms and functioning when we have more follow-up data to identify a sufficient sample of CHR participants who formally convert. In addition, we hope to examine crucial predictors of functional decline, regardless of diagnostic outcomes.

Regardless of whether or not these individuals convert to psychotic disorder, they are a help-seeking population, often experiencing significant distress, with significant functional impairment and high rates of mood and anxiety disorders (Meyer et al., 2005; Rosen et al., 2006; Cornblatt et al., 2007; Addington et al., 2011). If findings of the current study are replicated in future research, they point to the need for treatment aimed specifically at addressing depression and negative symptoms to improve functional outcomes in individuals experiencing attenuated psychosis. Psychosocial treatment trials have shown promise that treatment may significantly improve symptomatic and functional outcomes, even if conversion rates are not always significantly reduced (Morrison et al., 2004, 2007; Bechdolf et al., 2008; Addington et al., 2011; Kim et al., 2011). Although it is unclear which specific treatment approaches are most helpful (see Yung et al., 2010), our findings of the relation between depression and functional impairment suggest that treatments that directly address mood may be of significant benefit for individuals experiencing attenuated symptoms of psychosis.

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Contributors

RL, SV, DM, TN, and CC designed the study protocols. BS directed clinical assessment and associated data collection. DF conducted data analyses and conceptualized and wrote the first draft of the manuscript. EF coordinated data entry. All authors contributed to and have approved the final manuscript.

Conflict of interest

DM consults for Bristol Myers Squibb. CC has served as a one-time consultant for Pfizer, Merck, Lilly, Servier, and has received research funding from GlaxoSmithKline. SV is a paid consultant for Brain Plasticity Institute, Amgen, Hoffman La Roche, and Genentech. DF, TN, EF, BS, and RL declare no conflicts of interest.

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